NOT FOR PUBLICATION

UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF NEW JERSEY

THE MEDICINES COMPANY, Plaintiff, v. DR. REDDY'S LABORATORIES, LTD., DR. REDDY'S LABORATORIES, INC., and GLAND PHARMA, INC., Defendants.	Civil Action No.: 11-2456(PGS)(DEA) MEMORANDUM AND ORDER

SHERIDAN, U.S.D.J.

In this patent infringement case, the parties dispute the construction of six claim terms. After reviewing the parties' respective submissions and conducting a *Markman* hearing on October 2, 2012, the Court construes the disputed claim terms as set forth in subsection III below. *See Markman v. Westview Instruments, Inc.*, 52 F.3d 967 (Fed. Cir. 1995) (*en banc*), *aff'd* 517 U.S. 370 (1996).

I. BACKGROUND

Plaintiff, The Medicines Company, has filed a patent suit against Defendants, Dr. Reddy's Laboratories Ltd., Dr. Reddy's Laboratories, Inc. and Gland Pharma, Inc., for allegedly infringing U.S. Patent Nos. 7,582,727 (the "'727 Patent") and 7,598,343 (the "'343 Patent") (collectively, the "patents-in-suit"). The Medicines Company asserts that Defendants' Abbreviated New Drug Application ("ANDA") No. 201577, seeking approval to engage in the commercial manufacture and

sale of its generic Angiomax product, infringes the '727 and '343 patents. The patents-in-suit pertain to pharmaceutical formulations of bivalirudin and the processes of making bivalirudin. Bivalirudin is the active ingredient in Angiomax, which is a product marketed by The Medicines Company that is approved for use as an anticoagulant – a substance that prevents blood clotting – in patients undergoing coronary angioplasty.

The bivalirudin is manufactured into a finished drug product through a process referred to as "compounding." The first step involves forming a solution used to dissolve the bivalirudin, which is a powder (the "Part I solution"). The second step involves forming a solution of a base with a high pH (the "Part II solution"). The third step involves dissolving the Part I solution (containing bivalirudin), which has a low pH with the Part II solution to raise the pH, creating a "Part III solution." The resulting solution undergoes filtration before freeze drying to create a powder. Prior to administration, the powder is reconstituted into a liquid so that it can be injected into a patient. Original Angiomax was made using a different compounding process than the one claimed in the patents-in-suit. The Original Process resulted in inconsistent levels of impurities with higher incidences of the Asp^9 impurity. The high levels of Asp^9 impurity under the Original Process caused unpredictable batch failures and rejections, resulting in significant lost sales for The Medicines Company. The inventors of the patent-in-suit eventually developed a new compounding process. The patents in suit are directed at consistently minimizing the levels of the Asp^9 impurity generated during the manufacture of the drug product.

The disputed claim terms are: (1) "pharmaceutical batches"; (2) "aqueous solution"; (3) "maximum"; (4) "efficiently mixing"; (5) "wherein the batches have a pH adjusted by a base"; and

(6) "about". All six terms appear in Claim 1 of the '343 patent, and all but "efficiently mixing" appear in Claim 1 of the '727 patent. Claim 1 of the '727 patent, which is a composition claim, reads:

> 1. Pharmaceutical batches of a drug product comprising bivalirudin (SEQ ID NO: 1) and a pharmaceutically acceptable carrier for use as an anticoagulant in a subject in need thereof, wherein the batches have a pH adjusted by a base, said pH is about 5-6 when reconstituted in an aqueous solution for injection, and wherein the batches have a maximum impurity level of Asp^{9}-bivalirudin that does not exceed about 0.6% as measured by HPLC.

('727 patent, col. 25, ll. 56-64). Claim 1 of the '343 patent, a product-by-process claim, reads:

> 1. Pharmaceutical batches of a drug product comprising bivalirudin (SEQ ID NO: 1) and a pharmaceutically acceptable carrier, for use as an anticoagulant in a subject in need thereof, said batches prepared by a compounding process comprising:
>
> (I) dissolving bivalirudin in a solvent to form a first solution;
>
> (ii) efficiently mixing a pH-adjusting solution with the first solution to form a second solution, wherein the pH-adjusting solution comprises a pH-adjusting solution solvent; and
>
> (iii) removing the solvent and pH-adjusting solution solvent from the second solution; wherein the batches have a pH adjusted by a base, said pH is about 5-6 when reconstituted in an aqueous solution for injection, and wherein the batches have a maximum impurity level of Asp^{9}-bivalirudin that does not exceed about 0.6% as measured by HPLC.

('343 patent, Col. 27, ll. 13-31).

II. LEGAL STANDARDS FOR CLAIM CONSTRUCTION

There is a two-step analysis for determining patent infringement: "first, the court determines the meaning of the disputed claim terms, then the accused device is compared to the claims as

construed to determine infringement." *Acumed LLC v. Stryker Corp.*, 483 F.3d 800, 804 (Fed. Cir. 2007) (citation omitted). When the court engages in claim construction to determine the meaning of disputed claim terms, it is decided as a matter of law. *Markman v. Westview Instruments*, 517 U.S. 370, 372 (1996). It is well established that "[T]he construction of a patent, including terms of art within its claim, is exclusively within the province of the court." *Id.*

When construing claims, the court must focus on the claim language. As explained by the Federal Circuit:

> It is a bedrock principle of patent law that the claims of a patent define the invention to which the patentee is entitled the right to exclude. Attending this principle, a claim construction analysis must begin and remain centered on the claim language itself, for that is the language the patentee has chosen to particularly point out and distinctly claim the subject matter which the patentee regards as his invention.

Innova/Pure Water, Inc. v. Safari Water Filtration Sys., 381 F.3d 1111, 1115-16 (Fed. Cir. 2004) (citations omitted). When looking at the words of a claim, the words "are generally given their ordinary and customary meaning," which has been defined as "the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, i.e., as of the effective filing date of the patent application." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1312-13 (Fed. Cir. 2005).

The Federal Circuit has counseled:

> It is the person of ordinary skill in the field of the invention through whose eyes the claims are construed. Such person is deemed to read the words used in the patent documents with an understanding of their meaning in the field, and to have knowledge of any special meaning usage in the field. The inventor's words that are used to describe the invention – the inventor's lexicography – must be understood and

> interpreted by the court as they would be understood and interpreted by a person in that field of technology. Thus the court starts the decision making process by reviewing the same resources as would that person, viz., the patent specification and prosecution history.

Id. at 1313 (quoting *Multiform Desiccants, Inc. v. Medzam, Ltd.*, 133 F.3d 1473, 1477 (Fed. Cir. 1998)). Those resources, called intrinsic evidence, include the claim language, the specification, and the prosecution history. *See id.* at 1314.

However, when intrinsic evidence alone does not resolve the ambiguities in a disputed claim term, extrinsic evidence – evidence that is outside the patent and prosecution history – may also be used to construe a claim. *See id.* at 1317; *Vitronics Corp. v. Conceptronic, Inc.*, 90 F.3d 1576, 1582-83 (Fed. Cir. 1996). "[E]xtrinsic evidence concerning relevant scientific principles, the meaning of technical terms, and the state of the art" may be consulted; for example, expert testimony, dictionaries, and treatises. *Id.* at 1314. However, when a court relies on extrinsic evidence to construe a claim, the court should be guided by the principle that extrinsic evidence may never conflict with intrinsic evidence, because courts "have viewed extrinsic evidence in general as less reliable than the patent and its prosecution history in determining how to read claim terms." *Id.* at 1319. Thus, a court should take care to "attach the appropriate weight to be assigned to those sources." *Id.* at 1322-24.

III. ANALYSIS

A. Term 1 – "pharmaceutical batches"

For this term, Plaintiff proposed two definitions, referred to below as the Initial Proposal and the Alternative Proposal. Plaintiff's Initial Proposal was:

> A single batch, wherein the single batch is representative of all commercial batches, and wherein the levels of, for example, impurities represent levels for all potential batches made by said process, or all batches prepared by a same compounding process.

Plaintiff's Alternative Proposal was:

> "Batches" or "pharmaceutical batches" as defined herein may include a single batch, wherein the single batch is representative of all commercial batches (see generally, 3Manual of Policies and procedures, Center for Drug Evaluation and Research, MAPP 5225.1, Guidance on the Packaging of Test Batches at 1), and wherein the levels of, for example, Asp^{9}-bivalirudin, total impurities, and largest unknown impurity, and the reconstitution time represent levels for all potential batches made by said process. "Batches" may also include all batches prepared by a same compounding process.

According to Plaintiff, the Initial Proposal was meant to be a summary of the definition of the disputed term as set forth in the patents' specifications; the Alternative Proposal is the entire definition that appears in the specifications. *See* '727 patent, col. 5, ll. 27-36; '343 patent, col. 5 ll. 27-36.

Although the Defendants indicated in correspondence to Plaintiffs that they would not object to the Alternative Proposal, Defendants nevertheless retrenched on their concession and indicated that an introductory sentence, which appears in the patent specifications, was required. That introductory sentence reads, "As used here, 'batch' or 'pharmaceutical batch' refers to material produced by a single execution of a compounding process of various emobodiments of the present invention." According to Defendants, this introductory sentence is necessary to provide context for the Alternative Proposal.

Claim Construction

The Alternative Proposal is consistent with the specifications. *See* '727 patent, col. 5, ll. 27-36; '343 patent, col. 5 ll. 27-36. The Court adopts same, with minor changes, because the specification "acts as a dictionary" when it defines terms used in the claim. *Vitronics*, 90 F.3d at 1582. The Alternative Proposal references the Center for Drug Evaluation and Research's Manual of Policies and Procedures 5225.1–Guidance on the Packaging of Test Batches. The Court has reviewed the publication and determined that the reference is unnecessary in this context, as it merely provides support for a sentence in the Alternative Proposal that is clear on its face, and the reference may confuse the trier of fact.

A remaining issue is whether the introductory sentence from the patent specifications should be added to the construction. Defendants failed to set forth adequate support for their position that the preceding sentence is necessary. To the extent that the phrase "made by a compounding process," which appears in the introductory sentence, adds meaning to the term "made by said process," which appears in the Alternative Proposal, the added meaning does not clarify the construction. When viewed in the context of the specification, it is apparent that the phrase "made by said process" refers to the compounding processes described in the patents. An express antecedent basis for the term "said process" is not required here because the claim has a reasonably ascertainable meaning.

Accordingly, the Court adopts the following construction of the disputed term:

> "Batches" or "pharmaceutical batches" as defined herein may include a single batch, wherein the single batch is representative of all commercial batches, and wherein the levels of, for example, Asp^{9}-bivalirudin, total impurities, and largest unknown impurity, and the

> reconstitution time represent levels for all potential batches made by said process. "Batches" may also include all batches prepared by a same compounding process.

B. Term 2 – "aqueous solution"

Plaintiff argues that the term "aqueous solution" should be accorded its plain and ordinary meaning because it needs no construction, or in the alternative that it should be construed to mean "[a] liquid made by, with, or from water, including water." Defendants argue that the term should be construed to mean "[a] solution that includes water and at least one dissolved substance." Defendants argue that their proposed construction more accurately reflects the meaning of the term to persons of skill in the art because it takes into account that a solution is a solvent – in this case water – and a solute – "a substance that is intimately dispersed or dissolved within the solvent." Def. Markman Br. at 8. Plaintiff argues that its construction is supported by evidence in the intrinsic record that the liquid used for reconstitution includes water and can be water. The specification provides

> The injectable dosage form is prepared by reconstituting the pharmaceutical formulation in a pharmaceutically acceptable vehicle. Methods of reconstituting the pharmaceutical formulation are well known in the art. Pharmaceutically acceptable vehicles are also well known in the art and can include, but are not limited to, water and saline for injection. As an example, the injectable dosage form may be prepared by adding water to the pharmaceutical formulation and dissolving the pharmaceutical formulation. This solution can then be further diluted in 5% dextrose in water or 0.9% sodium chloride for injection.

'727 patent, col. 15, ll. 29-39; '343 patent, col. 15, ll. 31-41.

Claim Construction

Defendants' proposed construction does not allow for the possibility that the "aqueous solution" is comprised of water alone. This construction clearly conflicts with *Phillips* as it improperly excludes an embodiment – water alone – that is expressly described in the specification. *Phillips*, 415 F.3d at 1315-16; '727 patent, col. 15, ll. 29-39; '343 patent, col. 15, ll. 31-41. Plaintiff's proposed construction is supported by the evidence in the intrinsic record as it reflects the fact that the liquid used for reconstitution is water. However, Plaintiff's proposed construction includes the phrase "including water", which is redundant. Therefore, the Court construes the term "aqueous" to mean "a liquid made by, with, or from water."

C. Term 3 – "maximum"

Plaintiff argues that no construction is necessary, or that in the alternative the term should be construed as "upper limit." Defendants' proposed construction is "the highest level that can or will be produced." Defendants base their construction, in part, on a dictionary definition of the term defining "maximum" as an adjective – the way it is used in the claims – as "[h]aving or being the greatest quantity or the highest degree that has been or can be attained.." *American Heritage Dictionary* 1083 (4th ed. 2006). Defendants argue that their construction aligns naturally with the claim language and specification as they both use the term to refer to "the highest level of a specified characteristic." Def. Markman Br. at 9-10. Defendants also argue that the prosecution history supports their proposed construction because the patentees used the term "maximum" to distinguish the prior art.

Plaintiff argues that the term "maximum" does not require construction because it is not a technical term of art, its ordinary and customary meaning is readily apparent, the claim terms, specification and file history do not provide any alternative meanings, and there is no indication in the patent specification that the patent applicants chose to depart from the plain and ordinary meaning of this term. In the alternative, Plaintiffs argue that the term should be construed as "upper limit," which the Plaintiff derives from a dictionary definition which reads: "an upper limit allowed (as by a legal authority) or allowable (as by circumstances of a particular case)." *Meriam Webster's Collegiate Dictionary* (Frederick C. Mish et al. eds. 11th ed. 2004). Plaintiff argues that its proposed construction simplifies this dictionary definition without narrowing it. Plaintiff further argues that Defendants' proposed construction improperly limits the term, in that the proposed construction ignores the first portion of the dictionary definition that Defendants rely on; the dictionary definition Defendants rely on reads "having or being the greatest quantity or the highest degree that has been or can be attained", but the proposed construction ignores the first part of the definition – "having or being the greatest quantity" – and limits itself to the second part.

Claim Construction

The Court finds that this term does not require construction, and should be interpreted according to its plain and ordinary meaning. "Maximum" is not a technical term and its ordinary and customary meaning is readily apparent. There is no indication in the specification or file history that the patent applicants departed from the plain and ordinary meaning. Here, construction "involves little more than the application of the widely accepted meaning of commonly understood words." *Phillips*, 415 F.3d at 1314.

D. Term 4 – "efficiently mixing"

Plaintiff's proposed construction is "[m]ixing that is characterized by minimizing levels of Asp[9]-bivalirudin in the compounding solution." Defendants' proposed construction is "[m]ixing in a controlled manner under high shear mixing conditions." The term is found only in the '343 Patent, which is a product-by-process patent. A product-by-process claim defines the product "at least in part in terms of the method or process by which it is made." 3-8 *Chisum on Patents* § 8.05; *see also Abbott Labs. v. Sandoz, Inc.*, 566 F.3d 1282, 1293 (Fed. Cir. 2009) (*en banc*). "'[P]rocess terms in product-by-process claims serve as limitations in determining infringement.'" *Abbott*, 566 F.3d at 1293 (quoting *Atl. Thermoplastics, Inc. v. Faytex Corp.*, 970 F.2d 834, 846-47 (Fed. Cir. 1992)). "In determining infringement of a product-by-process claim, . . . the focus is on the process of making the product as much as it is on the product itself." *Amgen Inc. v. F. Hoffmann-La Roche, Ltd.*, 580 F.3d 1340, 1370 (Fed. Cir. 2009) (citing *Abbott*, 566 F.3d at 1293). "As a result, a product-by-process claim is not infringed by a product made by a process other than the one recited in the claim." *Id.* (citing *Abbott*, 566 F.3d at 1293).

Plaintiff's proposed construction is a functional definition of the term "efficiently mixing" – i.e. one that is focused on the outcome of the mixing process; Plaintiff wants the Court to define the term as mixing that produces a specific result. Defendants propose a process-based construction – i.e. one that specifies how to perform the process step; Defendants want the court to define the term as mixing that is performed in a particular way.

Plaintiff supports its construction with evidence from the intrinsic record. The specification of the patents-in-suit says, "Efficient mixing is characterized by minimizing levels of Asp[9]-

bivalirudin in the compounding solution." Plaintiff argues that the specification "acts as a dictionary" when it defines terms used in the claims. Pl. Markman Br. at 19 (citing *Vitronics*, 90 F.3d at 1582). Plaintiff further argues that claim terms may be functionally construed where the specification provides a functional definition and the claims and specifications do not recite a specific structural or process requirement. *Id.* (citing cases).

Defendants argue that the specification does not expressly define "efficient mixing," because the "characterized by" language is not meant to be definitional as can be seen by the fact that the definition portions of the specification explicitly define other terms using the phrase "refers to". *See e.g.*, Ex. 2, '343 patent, col. 5, ll. 37-55 ("The term 'drug product herein refers to . . ."; "The term 'formulation' or 'pharmaceutical formulation' refers to . . ."; "The term 'carrier' refers to . . ."). Defendants also argue that "[c]onstruing 'efficiently mixing' as [Plaintiff proposes] means any mixing that works and effectively reads 'efficiently mixing' out of the claims . . . [and] renders the 'efficiently mixing' claim term meaningless and superfluous," which would violate basic principles of claim construction. Def. Markman Br. at 15.

Defendants' proposed construction stems from their argument that the specification establishes that the two critical characteristics for efficiently mixing are: (1) how the pH-adjusting solution is physically added to the bivalirudin solution and (2) how the two are mixed together.

Regarding the method of adding the pH-adjusting solution, Defendants argue that it must be done at a controlled rate. Defendants say that Examples 3 and 5 in the specifications are the only two examples that the specification indicates have yielded the desired result of low levels of Asp^9-bivalirudin following the compounding process, and both examples state that the pH-adjusting

solution was added to the bivalirudin at a "controlled" rate. '343 patent, col. 21, ll. 3-5, col. 23, ll. 21-23. The specification provides a direct comparison of Example 5 to Example 4, where the process was said to have used "inefficient mixing", showing that the batches produced in Example 5 displayed significantly lower levels of Asp^9-bivalirudin. The Defendants also argue that the prosecution history suggests that uncontrolled addition of the pH-adjusting solution was outside the scope of the claims, because the patent applicants submitted materials explaining that their invention was, at least in part, a process improvement consisting of a "less subjective and more consistent process," and "wherein the base was added in a controlled . . . manner." Updated Accelerated Examination Support Document submitted on Nov. 26, 2008 in the '343 prosecution, at 3; April 6, 2009 Response to Rejection in '343 prosecution, par. 13.

Regarding the method of mixing the pH-adjusting solution with the bivalirudin, Defendants argue that it should be done under "high shear mixing conditions." This too, Defendant argues, is specified in the patent examples. According to Defendants, Examples 3 and 5 use fast, high shear mixing conditions and yield lower Asp-9 bivalirudin levels than do Examples 2 and 4. Defendants argue that Example 5, which uses high shear mixing, is the only example that is specifically identified as utilizing "efficient mixing" conditions.

Plaintiff argues that Defendants' proposed construction is inconsistent with the alleged "definition" in the specification and improperly attempts to impose limitations inconsistent with the intrinsic record. First, Plaintiff argues that Defendants' proposed construction fails to address the relationship between efficient mixing and the minimization of Asp^9-bivalirudin as stated in the specification. Second, Plaintiff argues that the proposed construction imports the limitations

"controlled manner" and "under high shear mixing conditions" from the specifications, which is improper because preferred embodiments and examples should not be used to limit claim scope as a matter of law. *See Innova*, 381 F.3d at 1117; *Transmatic*, 53 F.3d at 1277-78.

Claim Construction

The term "efficiently mixing" in the '343 Patent was recently construed in a separate litigation in the Northern District of Illinois. *See Meds. Co. v. Mylan Inc.*, 2012 U.S. Dist. LEXIS 109749 (N.D. Ill. Aug. 6, 2012) (hereinafter "*Mylan*"). The first point addressed in *Mylan* was the Plaintiff's contention that its proposed construction was set forth as a definition in the specification. For the reasons set forth in the *Mylan* opinion, 2012 U.S. Dist. LEXIS 109749, at *24-27, the Court finds that the patentees did not intend to expressly define the term "efficiently mixing" in the specification. If the patent applicants intended to expressly define "efficiently mixing" they could have put the term in quotation marks and inserted the words "refers to" or "as defined herein" after the term to clearly express their intent to define the term, as they did with other terms. *See Merck & Co., Inc. v. Teva Pharms. USA, Inc.*, 395 F.3d 1364, 1371 (Fed. Cir. 2005). However, just because Plaintiffs' proposed construction is not set forth as a definition in the patent specification does not mean that the construction is without merit.

The Court agrees with *Mylan* that the term "efficiently mixing" must be construed as part of a process step – i.e., as a term describing how to mix. *See Mylan*, 2012 U.S. Dist. LEXIS 109749, at *27-34. As *Mylan* points out, when read in context, the term "efficiently mixing" is part of the second step of a three-step process for producing the claimed pharmaceutical batches and must be construed accordingly. The first step in that process is "dissolving bivalirudin in a solvent to form

a first solution," the second step is "efficiently mixing a pH-adjusting solution with the first solution to form a second solution," and the third step is "removing' the solvent and the pH-adjusting solution solvent from the second solution." '343 Patent, Claim 1. As it is used in Claim 1 of the '343 Patent, the word "efficiently" modifies the "mixing" process step.

The Court, however does not think that adopting Plaintiff's proposed construction would read the "efficiently mixing" process step out of the claimed process. Plaintiff's proposed construction does not construe the claims of the '343 patent to capture pharmaceutical batches *made by any processes*; rather, Plaintiffs' construction defines one aspect of the claim's mixing step in a functional manner by saying that the resulting batches have minimized levels of Asp^9-bivalirudin. The proposed construction does not render that process step "meaningless." *Contra Abbott Labs v. Sandoz, Inc.*, 566 F.3d 1282, 1295 (Fed. Cir. 2009) (holding that product-by-process claim containing the phrase "obtainable by" could not be read to capture products obtainable by processes other than those explicitly recited in the claim because otherwise the process limitations chosen by the patent applicant to define its invention would be meaningless).

The Court agrees with *Mylan*, however, that in light of the '343 Patent specification and prosecution history the term "efficiently mixing" does not encompass the mixing process described in Example 4 in the specification. As the *Mylan* court describes in detail, the specification demonstrates that Example 4 did not achieve the goal of the invention – i.e., the process used in Example 4 did not compound bivalirudin while consistently minimizing impurities. *Id.* at *35-42. Accordingly, any construction of the term "efficiently mixing" that encompasses the mixing process described in Example 4 is incorrect, because "[w]here the specification makes clear that the

invention does not include a particular feature, that feature is deemed to be outside the reach of the claims of the patent." Honeywell Int'l, Inc. v. ITT Indus., *Inc.*, 452 F.3d 1312, 1319 (Fed. Cir. 2006) (internal quotation marks and citations omitted).

Having assessed Plaintiff's proposed construction, and having determined that the term must not encompass inefficient mixing conditions described in Example 4, the Court must now determine whether the additional limitations proposed by Defendant should be adopted. As stated above, Defendants argue that the specification establishes that the two critical characteristics of "efficient mixing" are: (1) how the pH-adjusting solution is physically added to the bivalirudin solution and (2) how the two are mixed together; Defendant further argues that the specification establishes that the pH-adjusting solution must be added at a controlled rate and the solutions should be mixed using high shear mixing. However, by importing the "constant rate" and "high shear mixing" limitations from the specification into the claims, Defendants commit a "cardinal sin" of patent law. *See Phillips*, 415 F.2d at 1319-20. The limitations are taken from Examples 3 and 5 of the patents, and the Federal Circuit has made clear that examples in the specification should not be used to limit claim scope. *Transmatic*, 53 F.3d at 1277-78. The specification clearly states that "efficient mixing" can be achieved by a variety of methods, including through the use of different mixing devices, by mixing at different speeds and temperatures, and by adding the two solutions together rapidly all at once, or in portions, or at a constant rate. *See, e.g.*, '343 Patent, col. 2, ll. 50-58; col. 8, l. 24-col. 11, l. 24. It is true that only the mixing methods in Examples 3 and 5, which were explicitly referred to as "efficient" mixing methods, achieved the desired result of minimizing levels of Asp^{9}-bivalirudin in the compounding solution. However, the specification lists many other methods of efficient

mixing besides those exhibited in Examples 3 and 5, and the Examples are preceded by the caveat: "the following non-limiting examples . . . are not intended, nor should they be interpreted to, limit the scope of the invention."

Under these circumstances, the Court does not agree with Defendant that the limitations found in Examples 3 and 5 should be imported into the claims by defining "efficiently mixing" as requiring the pH-adjusting solution be added at a constant rate under high shear mixing conditions.

The Court holds that the term "efficiently mixing" should be construed as "Mixing that is characterized by minimizing levels of Asp^{9}-bivalirudin in the compounding solution and that does not use mixing conditions described in Example 4." Negative limitations, which are generally not favored, are permissible when they are justified by clear disavowal or disclaimer. *Id.* (citing *Omega Eng'g, Inc. v. Raytek Corp.*, 334 F.3d 1314, 1322-23 (Fed. Cir. 2003) (declining to add negative limitation where district court and accused infringer did not identify "any express disclaimer or independent lexicography in the written description that would justify adding [the] negative limitation")); 3-8 *Chisum on Patents* § 8.06[3] ("[I]t is clear today that negative limitations are not impermissible per se . . . ."). Here, where the claim specification clearly disavowed the inefficient mixing processes used in Example 4, a negative limitation is proper.

E. Term 5 – "wherein the batches have a pH adjusted by a base"

Plaintiff argues that this term does not require construction by the Court and should be interpreted according to its plain and ordinary meaning, or in the alternative should be construed as "during compounding, the pH of the batches is adjusted using a base." Defendants argue that the term should be construed to mean: "Wherein during compounding of the batches a pH-adjusting

solution containing a base is added to a bivalirudin solution in a controlled manner under high shear mixing." The parties agree that the term "wherein the batches have a pH adjusted by a base" is used in the claims to describe the pH adjustment of the bivalirudin drug product during the compounding process. The specification of the patents-in-suit indicates that pH adjustment occurs during the compounding process:

> [O]nce the compounding solution is formed, the PH or the final volume of the compounding solution may be adjusted to a specified level . . . The pH or volume can be adjusted using methods known in the art, for instance, the addition of a pH-adjusting solution as described above.

('727 patent, col. 11, ll. 25-30; '343 patent, col. 11, ll. 25-30). The file history further confirms that the patent applicants made clear that the context for the pH-adjustment is the compounding step, as they stated that the "compounding process for bivalirudin drug product is generally performed by adjusting the pH of a bivalirudin solution from an initial acidic pH . . . to a desired pH range . . . ." '727 patent file history, at MEDDRL0001636-45 at 1640-41; '343 patent file history, at MEDDRL00000523-31 at 526.

However, Defendants' propose to add to the construction the limitation "in a controlled manner under high shear mixing." Defendants' position stems from their argument that the "alleged invention depends entirely on the process by which the pH-adjusting solution is added/mixed with the bivalirudin solution." Def. Markman Br. at 17 (emphasis added). In a rehash of their "efficiently mixing" arguments, the Defendants argue that the intrinsic evidence establishes that the pH adjustment must be done in a specific way – in a controlled manner under high shear mixing conditions – in order to produce pharmaceutical batches of bivalirudin with low impurities. The

Defendants argue that the specification and prosecution history show that (1) the production of Asp^9-bivalirudin during the compounding process was the problem that the inventors sought to solve, and (2) that efficient mixing – mixing at a controlled rate under high shear mixing conditions – was the only solution to this problem. Defendants argue that it was only after the patent applicants added the "wherein the batches have a pH adjusted by a base" limitation that the Patent Office lifted its anticipation rejection. Therefore, Defendants' argue that their proposed construction does not import limitations into the claims because their construction merely reflects what a person of ordinary skill in the art would understand the claim term to mean in light of the intrinsic evidence.

Plaintiff argues that Defendants' proposed construction imports limitations from the specification, in a rehash of their "efficiently mixing" arguments, but also that the construction blurs the distinction between the composition claims of the '727 patent and the product-by-process claims of the '343 patent. Plaintiff points out that the United States Patent and Trademark Office recognized the distinction between the '727 patent's composition claims and the '343 patent product-by-process claims during prosecution of these patents. Plaintiff argues that importing process steps into this term and turning the claims of the '727 patent into product-by-process claims would improperly require the '727 patent into product-by-process claims. *See K-2 Corp. v. Salomon S.A.*, 191 F.3d 1356, 1364 (Fed. Cir. 1999). In response, Defendants argue that the definition of "pharmaceutical batches" that applies to both patents refers to the process by which the claimed "pharmaceutical batches" are made ("produced by a single execution of a compounding process"). Therefore, Defendants argue, the claims of the '727 patent already include what amount to a process limitation, and as a result, a construction of the disputed term that includes the conditions of

"efficient mixing" does not add process limitations to the claims of the '727 patent, but merely gives meaning to the process that is already an integral part of the claimed "pharmaceutical batches."

Claim Construction

The Court construes the term to mean "during compounding, the pH of the batches is adjusted using a base." The intrinsic record supports this construction, and the parties agree on the fact that the pH adjustment referred to in the term occurs during the compounding process. Defendants' proposed construction would improperly rewrite the composition claims of the '727 patent as product-by-process claims, and would add process limitations to those claims.

F. Term 6 – "about"

Plaintiff asserts that this term requires no construction, and that it should be construed according to its plain and ordinary meaning. Defendant argues that it should be construed to mean "[a]pproximately with no more than a ± 0.1% deviation from the stated value." The term about appears in asserted claims 1-3 and 7 of each of the patents-in-suit.

Defendants' construction, which uses the dictionary definition "approximately" but which would allow a swing of nor more than plus or minus 0.1% in value, flows from the doctrine of claim differentiation. "Under the doctrine of claim differentiation, dependent claims are presumed to be of narrower scope than the independent claims from which they depend." *AK Steel Corp. v. Sollac*, 344 F.3d 1234, 1242 (Fed. Cir. 2003). Defendant argues that "if the 'about 0.3%' recited in claim 3 of the '727 and '343 patents were permitted to exceed 0.4% then claim 3 would subsume claim 2 from which it depends and which allows for maximum Asp^{9}-bivalirudin levels that do not exceed 'about 0.4%.'" Defendants' further argue that identical terms in separate claims should be afforded

the same construction, *see Southwall Techs., Inc. V. Cardinal IF Co.*, 54 F.3d 1570, 1579 (Fed. Cir. 1995), and thus the term "about" should be construed according to Defendants' proposal in each claim in which it appears.

Rather, Plaintiff argues that the term "about" needs no construction because it is not a technical term of art, its customary meaning is readily apparent, it is a commonly used patent claim term, and the specification and file history do not provide any alternative meanings aside from the ordinary and customary one, nor do they provide any indication that the patent applicants chose to depart from the ordinary meaning of this term. In the alternative, Plaintiff argues that should the Court decide that the term needs construction, Defendants' proposed construction is improper because "the use of the word 'about,' avoids a strict numerical boundary to the specified parameter," and should be construed as "approximately." *See Cohesive Techs., Inc. v. Waters Corp.*, 543 F.3d 1351, 1368 (Fed. Cir. 2008). Indeed, the District of New Jersey has consistently construed "about" to mean "approximately." *See e.g., AstraZeneca Pharms. LP v. Handa Pharms., LLC,* C.A. No. 08-3773, 2010 U.S. Dist. LEXIS 126078, at *12-15 (D.N.J. Nov. 30, 2010); *Teva Pharm. Indus. v. Dr. Reddy's Labs., Ltd.*, C.A. No. 07-2894, 2008 U.S. Dist. LEXIS 48039, at *22-23 (D.N.J. June 23, 2008). Plaintiff also argues that introduction of the limitation "with no more than a ± 0.1% deviation from the stated value" into the claim term is improper. Plaintiff argues that the proposed limitation is not in, nor is it suggested in, the specification or anywhere in the intrinsic record.

Claim Construction

The Court construes the term "about" to mean "approximately." There is no indication in the intrinsic record that a strict numerical range of ± 0.1% applies to this term. The claims of the

patents-in-suit demonstrate that the patent applicants deliberately intended to avoid a strict numerical boundary as they used the term "about" with respect to the maximum values of impurities. Had the patent applicants intended to include an exact numerical boundary, they would have done so. Defendants' reliance on claim differentiation is in error. Claim differentiation is generally employed to avoid rendering claims superfluous. However the claims in the patents-in-suit, claims 2 and 3 for example, would not be rendered superfluous merely as a result of overlapping scope. *See Anderson Corp. v. Fiber Composites, LLC*, 474 F.3d 1361, 1370. Therefore Defendants' attempted reliance on claim differentiation is rejected.

IV. CONCLUSION

The Court has reviewed the parties' submissions and has held oral argument on the disputed terms; and

IT IS on this 2nd day of January 2013 **ORDERED** that the following disputed terms shall be constructed as follows:

1. Term 1 – "pharmaceutical batches" – is construed as:

   "Batches" or "pharmaceutical batches" as defined herein may include a single batch, wherein the single batch is representative of all commercial batches, and wherein the levels of, for example, Asp^{9}-bivalirudin, total impurities, and largest unknown impurity, and the reconstitution time represent levels for all potential batches made by said process. "Batches" may also include all batches prepared by a same compounding process.

2. Term 2 – "aqueous solution" – is construed as "a liquid made by, with, or from water."

3. Term 3 – "maximum" – requires no construction.

4. Term 4 – "efficiently mixing" – is construed as "Mixing that is characterized by minimizing levels of Asp^{9}-bivalirudin in the compounding solution and that does not use mixing conditions described in Example 4."

5. Term 5 – "wherein the batches have a pH adjusted by a base" – is construed as "during compounding, the pH of the batches is adjusted using a base."

6. Term 6 – "about" – is construed as "approximately."

s/Peter G. Sheridan
PETER G. SHERIDAN, U.S.D.J.

January 2, 2013